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Delayed Hemolytic Transfusion Reaction Due to Anti-Go^a, an Antibody Against the Low-Prevalence Gonzales Antigen

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Go^a (D^{Cor}) is a low-frequency antigen in the Rh system found on red cells lacking part of the D mosaic (category IVa). Anti-Go^a has not been previously reported to cause hemolytic transfusion reactions. A 27-year-old African American male with sickle-cell disease, maintained on chronic transfusion, was noted to have dark plasma during an erythrocytapheresis, procedure, and the pretransfusion hemoglobin was noted to be 1 g/dl lower than 4 weeks before (with hyperbilirubinemia and a significantly increased LDH). Polyspecific direct antiglobulin test (DAT) was weakly positive (C3-weak, IgG-weak), and indirect antiglobulin tests (IATs) performed on the serum (pre- and posttransfusion reaction) and a red blood cell (RBC) eluate from the postreaction sample were negative. A segment from one of the four implicated units from the prior month's transfusion was strongly reactive at 37°C and using anti-human globulin (AHG) when crossmatched with the postreaction serum and the eluate. The postreaction serum, screened with a panel of red cells positive for low-prevalence antigens, reacted with three Go(a+) cells. The implicated unit was reactive with a previously identified anti-Go^a serum.

Key words: Rh, delayed hemolytic transfusion reaction, Go^a, sickle-cell disease

INTRODUCTION

The Go^a antigen was first described in 1956 as a low-frequency Rh antigen (D^{Cor}) found predominantly in persons of African descent [1]. In 1967, an antibody was identified in the mother of an infant with hemolytic disease of the newborn and was labeled as anti-Gonzales (Go^a), after the patient's surname [2]. Anti-Go^a recognized the previously described D^{Cor} antigen [3] (known in Rh nomenclature as Rh30 [4]). Go^a specificity is limited to category IV of the Tippett and Sanger classification [5] of D+ patients who make anti-D, and is the determinant that distinguishes category IVa from IVb (Go^a is found on red cells of category IVa persons) [3,6]. Prevalence of the antigen ranges from 1.85–2.8% among African Americans, and is <1% among Caucasian Americans [2,7]. Antibody to Go^a has been reported to cause hemolytic disease of the newborn [2,6]. However, there have been no reports of delayed hemolytic transfusion reactions (DHTR) due to anti-Go^a.

CASE REPORT

The patient is a 27-year-old African American male with sickle-cell (HbS) disease who has undergone monthly red blood cell (RBC) transfusions for 19 years as therapy for a cerebral vascular accident which occurred at age 8 years. At age 20, the patient was begun on partial exchange erythrocytapheresis to limit iron loading [8]. At the outset of transfusion therapy, the patient's red-cell antigen profile showed the presence of c, e, k, Fy^b, Jk^b, S, s, U, M, N, and P1, and the absence of C, E, K, Fy^a, Le^a, and Le^b. Eight years after the start of chronic transfusions, he had developed antibodies to E, K, Fy^a,

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TABLE I. Serological Reactions Which Identify Anti-Go^a as Causative of a Delayed Hemolytic Transfusion Reaction

		Rh-Hr								Kell		Duffy		Kidd		Lewis		P
Cell	Code	D	C	c	E	e	f	V	Cw	K	k	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P1
1	R1Rw 8086	+	+	0	0	+	0	0	+	0	+	+	+	+	0	0	+	+
2	R1R1 8115	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	0	+
3	rrJsa 7764	0	0	+	0	+	+	0	0	0	+	0	0	+	+	0	+	+
4	R1R1 158	+	+	0	0	+	0	0	0	+	w	0	+	+	0	0	0	+
5	rrV 477	0	0	+	0	+	+	+	0	0	+	0	0	+	+	0	+	+
6	rr N592	0	0	+	0	+	+	0	0	0	+	+	+	+	0	0	0	0
7	Ror D239	+	0	+	0	+	+	+	0	0	+	0	0	+	0	0	+	+
8	rr N897	0	0	+	0	+	+	0	0	0	+	+	+	+	+	0	+	+
9	rr 113160	0	0	+	0	+	+	0	0	0	+	+	+	+	+	+	0	0
10	R2r 504590	+	0	+	+	+	+	0	0	0	+	+	0	+	+	0	+	+
11	R1R1 B1121	+	+	0	0	+	0	0	0	0	+	+	+	0	+	0	+	+
12	Ro 6152	+	0	+	0	+	+	0	0	0	+	0	0	+	+	0	+	+
13	Ro 306371	+	0	+	0	+	+	0	0	0	+	0	0	+	0	0	+	+
14	Ro 310473	+	0	+	0	+	+	0	0	0	+	0	0	+	0	0	+	+
15	Transfused unit 1	+			0					0		0						
16	Transfused unit 2	+			0					0		0						
17	Transfused unit 3	+			0					0		0						
18	Transfused unit 4	+			0					0		0						

continued

Le^a, Bg^a, HLA-B13, HLA-Bw40, HLA-Bw37. His RBC exposure was >840 units between 1976–1995.

Dark plasma was noted by the operator during a discontinuous partial exchange erythrocytapheresis. The patient described mild lower back pain and low-grade fever during the previous 2 weeks. The hemoglobin drawn just prior to erythrocytapheresis was 1 g/dl lower than the pretransfusion hemoglobin 4 weeks before. Serum lactate dehydrogenase (LDH) was 4,137 U/l, and bilirubin was 3.6 mg/dl.

A direct antiglobulin test (DAT) performed on the postreaction sample was positive (C3-weak, IgG-weak), and an indirect antiglobulin test (IAT) performed with this serum using three reagent red cells showed no reactivity on immediate spin (IS) in saline, at 37°C and at antihuman globulin (AHG), with LoIon and PeG enhancement, or with Ficin pretreatment of the reagent red cells. (IATs performed monthly using LoIon enhancement over the previous 8 years had not revealed evidence of anti-K, anti-Fy^a, or anti-E, and the patient's last known exposure to units untested for any of these three antigens was 11 years prior to the DHTR.) An IAT (three reagent red cells) performed with an RBC eluate prepared from the postreaction sample was negative at AHG phase. Crossmatching of the postreaction serum and segments from the four donor units transfused 4 weeks prior to the reaction showed 4+ reactivity at AHG (LoIon- and PeG-enhanced) with one of these units (polyspecific DAT was negative on this unit) (Table I). Antigen typing of these four segments confirmed the red cells to be group O, D+, E−, K−, and Fy(a−). The postreaction serum was then tested against a panel of reagent red cells positive for low-frequency antigens, including C^w, Lu^a, Js^a, Kp^a, VS, Co^b, Go^a, Yt^b, Wr^a, Di^a, and M^g, and was reactive at 37°C (LoIon enhancement) and at AHG with the Go^a-positive red cell only (Table I). Three additional Go(a+) reagent red cells were tested with the postreaction serum, and the same reactivity was detected (Table I). The eluate also reacted with three Go(a+) reagent cells and with red cells from the donor unit that was strongly incompatible with the patient's posttransfusion serum, but did not react with the remaining three transfused units. Commercially prepared anti-Go^a was not available, but serum from another group O patient known to demonstrate anti-Go^a reacted at 37°C (2+) and at AHG (3+) with the implicated unit. Treatment of the postreaction serum with DTT reduced reaction strength at AHG to (2+), consistent with a mixed IgM and predominant IgG anti-Go^a. The initial crossmatch with the Go(a+) unit 4 weeks prior to the reaction was negative at IS, 37°C (LoIon), and AHG. This pretransfusion sample was not available for repeat testing; however, a serum sample from the patient, frozen 2 years before, did not react at IS, 37°C (LoIon), or AHG with three Go(a+) reagent cells or with the implicated donor unit.

DISCUSSION

This patient had previously made antibodies to at least six RBC antigens, including E, K, and Fy^a. The probabilities of finding donor units lacking these three clinically significant antigens from Caucasian or African American

TABLE I. Serological Reactions Which Identify Anti-Go^a as Causative of a Delayed Hemolytic Transfusion Reaction (Continued)

									Serum (1/95)			Serum (8/93)					Anti-Go^a serum		
		MNSs				Lutheran				Lo-Ion			Lo-Ion		Eluate (1/95)			Lo-Ion	
Cell	Code	M	N	S	s	Lu^a	Lu^b	Other	IS	37°C	IgG/CC	IS	37°C	IgG/CC	Wash	IgG/CC	IS	37°C	IgG/CC
1	R1Rw 8086	0	+	0	+	0	+	Cw	0	0	0/+								
2	R1R1 8115	+	0	0	+	+	+	Lu^a	0	0	0/+								
3	rrJsa 7764	+	+	0	+	0	+	Js^a	0	0	0/+								
4	R1R1 158	+	+	0	+	0	+	Kp^a	0	0	0/+								
5	rrV 477	0	+	0	+	0	+	VS	0	0	0/+								
6	rr N592	+	0	+	0	0	+	Co^b	0	0	0/+								
7	Ror D239	+	0	+	0	0	+	Go^a	0	3+	3+								
8	rr N897	+	+	+	+	0	+	Yt^b	0	0	0/+								
9	rr 113160	0	+	0	+	0	+	Wr^a	0	0	0/+								
10	R2r 504590	+	0	0	+	0	+	Di^a	0	0	0/+								
11	R1R1 B1121	+	0	+	+	0	+	M^g	0	0	0/+								
12	Ro 6152	0	+	0	+	0	+	Go^a	0	3+	3+	0	0	0/+	0/+	1+			
13	Ro 306371	+	+	+	+	0	+	Go^a	0	3+	3+	0	0	0/+	0/+	1+			
14	Ro 310473	0	+	+	+	0	+	Go^a	0	3+	3+	0	0	0/+	0/+	1+			
15	Transfused unit 1								0	0	0/+	0	0	0/+					
16	Transfused unit 2								0	0	0/+	0	0	0/+					
17	Transfused unit 3								0	0	0/+	0	0	0/+					
18	Transfused unit 4								0	3+	3+	0	0	0/+	0/+	1+	0	2+	3+

donors would be 0.22 and 0.70, respectively [9].[1] The donor base in our region is comprised of 10% African Americans (personal communication, D. Moolten, American Red Cross—Penn Jersey). Selecting units lacking the E, K, and Fy^a antigens increases the chance of transfusion a unit of blood from an African American donor to 26%.[2] Since the prevalence of Go^a among African-American donors is 1.9–2.8% and essentially zero among others, the probability of exposure to the Go^a antigen from our donor pool would be 1 in 357–526 units without selection for E−, K−, and Fy(a−) units,[3] and 1 in 137–204 with selection.[4] Thus, antigen matching in this patient increased the chance of exposure to the Go^a antigen by 2–3-fold.

The serological findings on the postreaction sample confirm the presence of an IgG anti-Go^a in this patient's serum and on circulating RBCs. The pretransfusion crossmatch of the implicated unit (1 month prior) was negative. Dark plasma, the presence of complement on RBCs from the posttransfusion reaction sample, and the observation that DTT treatment of the postreaction serum diminished reactivity at AHG phase, all suggest an IgM component to the immune response. These findings are most consistent with a brisk primary immune response with both IgM and IgG components detectable 4 weeks following transfusion of Go(a+) RBCs. Alternatively, an anamnestic response to the Go^a antigen could explain the serological findings.

[1]Antigen frequencies Caucasians: E(−) 0.72, K(−) 0.91, Fy(a−) 0.34; African Americans E(−) 0.79, K(−) 0.98, Fy(a−) 0.90.
[2]Probability of finding antigen negative unit from African American donor = (0.70)(0.10) = 0.07; from Caucasian donor = (0.22)(0.90) = 0.20.
[3](1.9%) (0.10) = 0.0019 = 1/526.
(2.8%) (0.10) = 0.0028 = 1/357.
[4](1.9%) (0.26) = 0.0049 = 1/204.
(2.8%) (0.26) = 0.0073 = 1/137.

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